Major Program

Major program serves the major needs of the national economy and sustainable development of the society and S&T development. By selecting scientific issues with strategic significance, it integrates innovative human resources, conducts multidisciplinary research, and plays the leading and guiding role of further improving the capability of making indigenous innovation in China's basic research.

Major Program projects will be implemented by unified planning and supporting research projects in batches. Research areas for Major Program will be proposed on the basis of in-depth discussions and soliciting opinions among scientists according to NSFC priority areas. It focuses on the growth points resulting from long term funding of NSFC projects, and aims at achieving important breakthroughs in key scientific problems through high level funding.

NSFC only accepts integrated applications for each Major Program, which should include both the overall application for the Program and proposals for research projects. Please pay attention to relationships between various projects. Proposals involving only part of the research areas or one of the research projects indicated in the Guide of each Major Program will be not accepted. Each application can contain no more than 5 projects (please see the Guide to Major Programs for details), and in general one project should be carried out by one unit, and may not be more than 2 collaborative research units. Collaborative units may not exceed 5, and the applicant must be one of the PIs of the projects proposed.

Applicants should have the following qualifications:

(1) Have experience of undertaking basic research projects;
(2) Have senior academic position (title).

Researchers working in post-doc stations or graduate students are not qualified to apply.

Applicants should follow the guidelines when writing proposals. "Major Program" should be selected in the funding category and "application for Major Program" or "proposals for projects" in the sub-category, and the research area of the Major Program should be indicated in the annotation.

Proposals with incorrect selections will be not accepted.

In 2013, the guidelines of 4 Major Program projects have been announced in the second group of the Twelfth Five-Year Plan. Accordingly proposals should be refined on key scientific issues with strategic and fundamental significance and put forward clear, concentrated and interdisciplinary scientific targets, and pay attention to coordinate and link with other national S&T programs. The research team should have good accumulation of research work, sufficient research conditions and ability of making innovations, and a number of high level academic leaders. Each project will be funded with 15-20 million yuan for 5 years.

Research on the Metabolic Mechanism and Engineering of Industrial Biocatalysts

The conventional modification of industrial biocatalysts is mainly concerned on modifying the carbon metabolism by adapting the enzymes involved in metabolic pathways to improve the enzyme activity and block or reduce the by-product or construct new metabolic pathway. Such modification has in principle solved problems in the construction of metabolic network and the regulation of related enzymes. However, the mechanisms and regulation rules of the co-factors involved in the cellular metabolic network including signaling transduction, energy transfer and oxidation-reduction capacity remain poorly understood. As an outcome of limited research on the regulatory mechanisms of co-factors on the integrated metabolic flows, and gene transcription and expression, the modifications often fail to meet the expectations and become the bottleneck hindering the propagation of large-scale bio-manufacturing.

This project targets the research on the metabolic mechanism and engineering of industrial biocatalysts and focuses on the two key scientific issues: “regulatory mechanisms of co-factors and carbon metabolism” and “engineering and optimization of highly efficient biocatalysts”. From the perspectives of genomics, transcriptomics and metabolomics, the influences and functional mechanisms of co-factors on the gene transcription and expression, and the regulation of carbon metabolism will be investigated in order to reveal the key kinetic nodes and rate limiting steps in the metabolic pathways and provide theoretical foundations for the optimized assembly of functional modules in the pathways. The aims of project are to design the metabolic pathways according to the information of system biology, to

rationally devise and reconstruct the regulatory elements of co-factors, to fine tune the adaptation of the metabolism and the co-factors, and in turn to build the methodology of high efficient biocatalyst engineering and lay the foundation of the applied key engineering projects such as the original 'high efficient biofuel' and 'bio-produced substitutes of chemicals', and develop new demonstrative industrial technology with low energy consumption, less material usage and reduced waste emission.

I. Scientific targets

Due to the problems of low conversion ratio, low reaction rate and low productivity, researches on the new generation of biocatalysts are performed from the perspectives of metabolic mechanisms of industrial biocatalysts and optimized high efficient biocatalyst engineering. The synergistic rules between co-factors and carbon metabolism, and the influences of co-factors on the regulation of carbon metabolic flows and cellular gene expression need to be elucidated, in order to develop the systematic theory on the adaptation and regulation of biocatalysts and provide new research directions of highly efficient industrial biocatalyst engineering. Through the basic science research in metabolic mechanisms of high efficient industrial biocatalysts, the synthesis of biofuels such as butanol and ethanol, bulk chemicals such as Vitamin C and lactic acid, fine chemicals such as amino acid and nucleotide, can be alternatively produced in a manner with low energy consumption, less material usage and reduced waste emission. The newly developed technology would be clean and highly efficient with proprietary intellectual property rights, and would effectively promote the development of industrial biotechnology in China.

II. Research contents

Based on the academic blueprint of the project and targeted at the key scientific issues, the research will be performed in the five aspects as follows.

1. Model construction of new generation metabolic network

According to the database information from genomics, proteins and enzymes, mesostates, biochemical reactions, carbon metabolic pathways and co-factor metabolism, an interaction network model of genes, proteins, biochemical reactions and co-factors can be proposed. The foundation of the regulatory model of co-factor metabolism can be laid through the simulation and analysis of gene regulatory network, signaling conduction network and protein-protein interaction and metabolic network.

2. Study on the mechanism of how co-factors regulate gene expression and metabolic flow

Study the genomic sequence information of microbes and the regulatory laws of gene transcription at cellular level; identify the expression, modification, structure, function and interaction of proteins; analyze the allocation of metabolic flow; integrate the – omics data to investigate the mechanism of co-factors on the regulation of carbon metabolism and gene expression and build regulatory network model with significantly enhanced predictive capacity. Perform the analysis of metabolic regulation focusing on the biosynthesis pathway of target chemical compound, important pathways in the metabolic network and key nodes at bifurcation, turbulence of co-factors towards metabolic flow at nodes and concentration of mesostates, reveal the key kinetic nodes and rate limiting steps in the metabolic pathways, and provide theoretical foundations of how co-factors regulate metabolism.

3. Design the optimized synthesis pathway of the target chemical compound

All possible metabolic pathways towards a given chemical compound can be achieved based on relevant database information. Through strategies of simulation of the metabolic thermokinetics, or reducing power balance, the most feasible metabolic pathway will be selected. Within a single microbe or in-vitro, by expression of enzymes from different origins or combination of the metabolic pathways from different organisms, and by genetic modifications of the enzymes, new metabolic pathways equipped with new function can be engineered to produce bulk chemicals, fine chemicals and biofuels.

4. Systematic construction and characterization of metabolic regulation of co-factors

Biofuels such as butanol, bulk chemicals such as Vitamin C, fine chemicals such as Lysine and adenosine cyclo-phosphate, can be utilized as research objects to build the regulatory strategy that combines co-factors and metabolism. Considering the optimized design of synthesis pathways, analyze and decouple the modules and compose the principle of module assembly. Fast screen the motif with highest catalytic activity by data-mining, and further improve its catalytic activity by rational design and directed evolution. Based on the functional characterization of motifs, build the motif library catalyzing a variety of biochemical reactions.

5. Adaptation and optimization of metabolism and co-factor

By comparing the different requirements on co-factors in the metabolic pathways of the synthesis of chemical compounds including butanol, Vitamin C and adenosine cyclophosphate, adapt the metabolic pathways from microbes such as yeast, bacillus and fungus through gene modification or environmental stress, in order to kinetically match the carbon metabolic pathways and co-factor metabolic pathways, release the feedback repression or suppression effect, and redistribute carbon substance. As a result, the efficiency of artificially cellular- synthesized target products can be improved and alternative synthesis pathways for part of the products can be achieved. In the scale of industrial manufacturing the production efficiency should be increased more than 30%, but the energy consumption and waste emission should be decreased more than 30%.

III. Funding period

5 years (from Jan. 2014 to Dec. 2018)

IV. Funding

Total 18 million yuan

Source, Fate, Human Population Exposure, and Health Risk of Typical Semi-volatile Persistent Organic Pollutants in Eastern China

Due to their wide environmental occurrence and significant hazards to human health, persistent organic pollutants (POPs) are one of the most important pollutant classes of global concern. Polycyclic aromatic hydrocarbons (PAHs), organochlorine pesticides (OCPs), and polybrominated diphenyl ethers (PBDEs) are representatives of typical POPs and therefore have been targeted by the Stockholm Convention and the Geneva Long Distance & Boundary-Beyond Air Pollution Convention. Moreover, the National Mid- and Long-Term Scientific and Technological Development Plan and the Twelfth Five-year Development Plan also include research initiatives on POPs.

At present, pollution of China’s environments by these POPs is quite severe, and the situation is particularly urgent in eastern China with great pollutant emissions and high population density.

Environmental behavior and regional processes of POPs are emerging multidiscipline domains of international environment research. To date, there is still a knowledge gap on some fundamental issues, such as large-scale regional spatial-temporal distributions of emission sources of the target POPs, kinetics of air-land exchange processes, quantitative relationship between source and sink, human population exposure patterns, and quantitative characterization of health risk. In-depth studies to systematically, comprehensively and quantitatively understand the generation, multimedia environmental behavior, regional transport and fate, and human exposure and health risk of POP, are a prerequisite for formulating rational control measures and effective constraints on health hazards.

I. Scientific targets

With the typical POPs as target compounds and the regional environmental processes in East China as the core scientific issue, this proposed project will conduct investigations to fulfill key knowledge gaps on regional environmental processes, and systematically and quantitatively elaborate the main emission sources and amounts of PBDEs, OCPs, and PAHs in East China, their transportation and transformation patterns in multimedia environments, dominant pathways entering foodstuff, and exposure amounts via inhalation and dietary intake for human population and related health risk.

II. Research contents

1. Main emission sources and inventories of the target POPs

The objective is to ascertain the main sources and emission characteristics of PBDEs, PAHs and OCPs in the study region, determine their emission flux and establish regional-scale emission inventories, and explore the spatial distribution patterns of emission densities and origins and predict the temporal trends of emissions.

2. Pollution characterization and source-receptor relationship

The objective is to describe the concentration levels, spatial distribution patterns, and dynamic variability of the target POPs in the main environmental compartments of the study region, explore the prevailing factors influencing the spatial-temporal heterogeneity in contamination levels and formation mechanisms, simulate the temporal trends and potential

impacts of climate change on the spatial-temporal variations, reveal the exchange patterns of the target POPs between the main environmental compartments and influencing factors, and investigate the quantitative relationships between emission sources and principal environmental sinks and the governing factors.

3. Atmospheric transport and human inhalation exposure risk

The objective is to examine the mechanism governing exchange of the target POPs between indoor and outdoor environments, establish an atmospheric transport-multimedia exchange coupling model to quantitatively simulate the transport processes of the target POPs in the study region and surrounding areas so that the atmospheric fate of the POPs can be revealed, quantitatively characterize the long distance transport, outflow and trans-boundary transport potential of the target POPs, and determine the characteristics of human inhalation exposure to the target POPs in the study region and the health risk of human population through inhalation exposure.

4. Accumulation in foodstuff and exposure risk of human population via dietary intake

The objective is to explore the chief pathways of the target POPs entering the main vegetative and animal foodstuffs, understand the magnitude of pollution by the target POPs in main foodstuffs in the study region, clarify the prevailing reasons responsible for the regional differences in food pollution, reveal the transfer characteristics of the target pollutants with the main foodstuffs in the study region, examine the bioavailability of foodstuffs-derived POPs in human gastro-intestinal tract, determine the patterns of human exposure via diet intake and the related spatial and temporal variability, and analyze the health risk of human population through dietary intake.

Ⅲ. Funding period

The funding duration for the project is 5 years (from January 2014 to December 2018).

IV. Funding

The funding amount for the project is 20,000,000 RMB.

Research on the Economic, Social and Environmental Coordinated Development of the Modern Logistics Management

The social, economic and environmental coordinated development of the human society has become the inevitable choice of sustainable development. The logistics industry of the national economy as an important industry plays an important role in supporting and protecting economic and social development. While promoting economic and social development and improving the level of human life, logistics also caused negative effects to the environment that cannot be ignored. Therefore, the modern logistics must take the social, economic and environmental coordination optimization as the management goal, and must make the decision and operation under the restriction of all sorts of relevant laws and regulations and standards.

During the rapid growth in the overall size and expansion of infrastructure of the logistics industry in China, there still exposes problems as the rules and regulations are not perfect, and problems of low logistics efficiency, high cost, low level of safety and quality are still to be solved. The demands of modern era on coordinated development of economy and society and environment and the development of logistics industry in China are sure to call for innovative development in modern logistics theory and technology.

At present, basic scientific problems such as the logistics system in the economic, social and environmental coordinated development, promoting green logistics through government control mechanism and enterprise competitive strategy needs to be further studied urgently. Frontier management technology to adapt the coordinated development of new logistics innovation, multimodal transport, low carbon and security logistics, urban logistics is also to be developed.

Through the integration of multi-disciplinary research strength in China, according to major practice of China's economic and social development, conduct research on economic, social and environmental coordinated development of the modern logistics management, solve some key scientific and technological problems in the forefront field. This will promote the development of related disciplines and high level research teams, and effectively promote research level of the logistics management and management discipline.

Ⅰ. Scientific targets

Further study will be focused on important scientific problems in the economic, social and environmental coordinated development of the modern logistics based on realistic background of China's economy, society and environment and logistics practice, taking account of new features of modern logistics and combined with advanced information technology: through the study of logistics system, the behavior of participants and decision theory, find out new laws of logistics innovation that promotes the coordinated development; according to our country's economic and social reform practice, develop multimodal transport and logistics infrastructure operation management theory, propose some methods and techniques of low carbon and safe logistics and city logistics management.

According to the transformation mode of economic development and the great demand of guaranteeing and improving the livelihood of people, carry out research on typical logistics system like the multimodal transport logistics, new energy logistics and urban logistics, and promote close linkage between modern logistics theory innovation and application practice, as well as China's economic, social and environmental coordinated development, build up a interdisciplinary research team influential at home and abroad.

Ⅱ. Research contents

1. The basic theory of logistics system on the economic, social and environmental coordinated development

According to the objective laws of human economic and social development and the requirements on green development, combined with China's important practical problems, develop logistics system theory, the behavior of participants in green logistics system and system design theory facing the social change of global economy. Key issues include: formation mechanism and evolution of the global logistics network under the background of economic globalization; domestic integrated logistics connecting the world; logistics set match theory on the economic and social changes; the behavior of participants in green logistics system and multilayer decision theory; logistics system designs under the restriction of the environment, safety regulations and standard; logistics infrastructure investment, financing mode and service pricing research.

2. Innovation research on promoting economic, social and environmental coordinated development of the logistics

Study the characteristics of modern logistics innovation and transformation mechanism, modern logistics and new energy logistics innovation theory in low carbon environment according to the social, economic and environmental coordinated development needs, combined with modern information, renewable energy and other emerging technology and the development of China's logistics practice. Key issues include: logistics innovation mode under economic development and environmental change, evaluation method of logistics innovation ability; logistics form change rule and transformation mechanism research to adapt to the social, economic and environmental development, the influence of information technology in logistics innovation mode and value creation mechanism analysis; biomass energy logistics management mode innovation and network design; the logistics management innovation and policy evaluation under the restriction of carbon resources; "carbon neutral" service and logistics integration innovation research.

3. Multimodal transport logistics operation management

Study the multimodal transport logistics operation management according to human economic, social and environmental coordinated development in China and the requirements of the green development and building a resource-conserving and environment-friendly society's development strategy, combined with the present situation of China's comprehensive transportation. Key issues include: comprehensive impact analysis of multimodal transport operation mode to economic, environmental and social; green operation disorder analysis of logistics terminal infrastructure; logistics operation management supporting multimodal transport under the carbon emissions constraints; logistics terminals' multimodal transport logistics service cooperation operation management; international logistics operation management of container multimodal transport; dynamic logistics terminal multi-stage logistics task assignment; and the interruption management of multimodal transport logistics.

4. Low carbon and safe logistics operation management

To create a green and safe future world, the logistics industry is promoting low carbon economy through the management and technology innovation, ensuring the safety and health of human life, thus to realize the sustainable development of society and economy. Key issues include: the safety analysis and safety operation management during logistics transport; low carbon operation strategies and methods of the logistics system; the low carbon

logistics cooperation operation considering the parties and multiple attribute; reverse logistics management in low carbon environment; the control and operation strategy of food logistics safety and quality in the whole life cycle.

5. Urban logistics management

Develop urban logistics management theory, method and evaluation system of research according to our cities' high speed development and the economic, social and environmental coordinated development needs, in view of the new problems of mega metropolitan logistics management and combined with information technology. Key issues include: the city logistics demand and its evolution analysis; city logistics hub layout and dynamic coordination management; logistics intelligent traffic management and control facing the city; city logistics resources integration and public distribution based on the information; the urban express logistics cooperation operation management under the network environment of; city logistics policy design and performance evaluation.

Ⅲ. Funding period

The funding duration for the project is 5 years (from January 2014 to December 2018).

Ⅳ. Funding

The funding for the project is 15 million Yuan.

Pathogenesis and Development of Glucose Metabolic Homeostasis Imbalance

Glucose metabolic homeostasis imbalance is the common basic path-physiological mechanism of several important metabolic diseases such as insulin resistance and type 2 diabetes. Along with the improvement of the living standards of Chinese people, there are dramatically increase of the prevalence of diseases with glucose metabolic disorder. Take diabetes as an example, the conservative estimation of the diseased people is 97 million at present in our country, which account for 9.7% people in China. The increased case number of diabetes patients in China is still going up without effective control till now. The cardiovascular, renal, brain and eye-vascular complication of diabetes can not only have severe impact on the living

qualities of the patients, but also bring heavy burden on family and social health care. Therefore, the prevention and treatment of glucose metabolic related diseases is a major scientific issue of our country nowadays. It is the major demand of our country at present to investigate the new mechanisms and control of the glucose metabolic homeostasis imbalance.

This Major Program project is based upon the epidemiological and clinical research achievements, combining the strengthen of basic research of our country, enclosing the regulatory mechanism of glucose metabolic homeostasis, to investigate the transcriptional and post-transcriptional regulation of genes involved in glucose homeostasis, to investigate the insulin signaling and pathogenesis of insulin resistance, to investigate the role of periphery tissue such as liver, intestine, fat and muscle on pancreatic beta cell mass, to investigate the role of meta-inflammation and glucose homeostasis, to investigate thoroughly the gene regulatory network involved the glucose metabolic homeostasis, in order to elucidate the scientific evidence of the mechanisms of insulin resistance and type 2 diabetes. By support of this project, new important therapeutic targets may be found for diseases related to glucose metabolic homeostasis imbalance and further develop therapeutic medicine for diabetes.

Ⅰ. Scientific targets

Based upon the present findings by the scientists of our country, focusing the major scientific problems in basic research of prevention and treatment of glucose metabolic disorder related diseases, to elucidate the possible new mechanisms of the pathogenesis and development of glucose metabolic homeostasis imbalance, by investigating thoroughly on the transcriptional and post-transcriptional regulation of genes involved in glucose homeostasis, on the insulin signaling and pathogenesis of insulin resistance, on the role of periphery tissue on pancreatic beta cell mass and on the role of meta-inflammation and glucose homeostasis.

Ⅱ. Research contents

1. Transcriptional and post-transcriptional regulation of genes involved in glucose metabolic homeostasis
2. The amount of pancreatic beta cell mass, insulin secretion, insulin signaling and pathogenesis of insulin resistance
3. The role of periphery tissue-pancreas axis on the regulation of blood glucose metabolic homeostasis
4. The role of meta-inflammation on glucose metabolic homeostasis

Ⅲ. Funding period

The funding duration for the project is 5 years (from January 2014 to December 2018).

Ⅳ. Funding

The funding for the project is 18 million yuan.